

Application No. 09/481,572
Am dt Dated: June 16, 2005
Reply to Office Action of March 16, 2005

REMARKS/ARGUMENTS

Reconsideration and allowance in view of the interview of March 2, 2005, as well as the following amendments and remarks are requested.

Claims 1, 8, 10, 23, 26 and 28-44 were pending in this application. Claims 26, 28 and 31-38 have been withdrawn from consideration. Claim 29, drawn to the treatment of ischemic condition was deemed to be allowed in the Examiner's December 6, 2004 Office Action. Further, on page 2 in the Examiner's March 16, 2005 Office Action, the Examiner indicated that no prior art was found on ischemic condition. Accordingly, such claim was mistakenly indicated to be withdrawn in the present Office Action when such claim should have correctly been deemed allowed. By this Amendment, Applicants have cancelled claims 1, 8, 10, 23, 26 and 28-44 without prejudice and have added new claims 45-64. Support for the new claims can be found in the specification and claims as originally filed. The new claims introduce no new matter, and thus, their entry is respectfully requested. Upon entry of the present Amendment, therefore, claims 45-64 will be pending and under examination.

This Amendment follows a personal interview held March 2, 2005 between Applicants' undersigned attorneys, Steven M. Giovannetti and Monica C. Kits, and Examiner Michael Meller. The courtesies extended Applicants' attorneys during the Examiner interview are sincerely appreciated. The Remarks presented in this Amendment make of record and further address the issues discussed during the interview.

The new claims presented herein clearly recite a novel therapeutic use of an extract from Hypericum perforatum (Hp extract) which is not disclosed in the cited art. Specifically, the new

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claims are directed, *inter alia*, to a method of inhibiting T-type calcium channels in a patient's cells comprising administering to a patient in need of such inhibition a composition comprising an amount of an extract from *Hypericum perforatum* effective to inhibit the movement of calcium ions into cells. Such a use for an Hp extract is not disclosed in the cited art, nor is it obvious in view of the cited art since the cited art does not teach or suggest that Hp extract would have an inhibitory effect on T-type calcium channels. Further, the cited art does not teach or suggest how an Hp extract could be administered in order to exert such a specific effect or that an Hp extract can be used to treat the claimed health disorders associated with T-type calcium channels. Indeed, the present inventors have unexpectedly found that Hp extracts can exert an inhibitory effect on T-type calcium channels and thus, inhibit the movement of calcium ions into cells.

Elections/Restrictions

The Examiner restricted Claims 1, 8, 10, 23, 26 and 28-44 into three groups in his August 13, 2004 Office Action. As discussed during the interview, and reflected in the Interview Summary and subsequent March 16, 2005 Office Action, the Examiner agreed that the outstanding restriction requirement was improper and would be vacated. Accordingly, all pending claims were examined together. (See attached Interview Summary).

Claim Rejection under 35 U.S.C. § 112

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Claims 1, 23, and 44 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Applicants believe that the addition of new claims 45-64 fully overcomes the Examiner's concern, and it is respectfully submitted that claims 45-64 comply with the requirements under 35 U.S.C. §112, second paragraph. Further to the discussion during the interview, the claims now clearly indicate to whom the Hp extract is being administered. Also, new dependent claim 49 clearly indicates that the claimed extract therein is a methanol or ethanol extract of Hp. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, second paragraph.

Claim Rejection under 35 U.S.C. § 102

Claims 1, 8, 10, 23, 30, 39-44 stand rejected under 35 U.S.C. §102(e) as being anticipated by Khwaja et al.

Because the Examiner's initial search turned up no prior art related to the treatment of ischemic condition using Hp extract (see page 2 of March 16, 2005 Office Action), the Examiner searched for art related to the treatment of arrhythmia using Hp extract. The Examiner contends that Khwaja et al. teaches the use of an Hp extract to treat arrhythmia.

In response, Applicants maintain that the claimed method for treating arrhythmia, as well as the other claimed health disorders, is not anticipated by Khwaja et al. As thoroughly discussed

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in the interview, Applicant submits that Khwaja does not tie Hp extract to the treatment of arrhythmia or any of the other health disorders listed in the present claims, and it does not teach or suggest that it would be desirable to treat such health disorders using Hp extract. Indeed, Khwaja teaches an invention, which "provides the ability to closely control the quality, dosage and clinical effectiveness of botanical extracts and other botanical materials, e.g., botanical of St. John's Wort," by establishing chemical and/or bioactivity fingerprint standards for various botanical materials. (Col. 12, lines 37-40). Khwaja goes on to discuss the methods of processing and extracting botanical materials in general. (Col. 19, Sec. 5.2). Khwaja also discusses the establishment of appropriate bioassays, where the combination of such bioassays, "will depend upon the complexity of the given botanical material and its intended clinical use." (Col. 23, line 3-5). Khwaja merely gives a general list of possible assays (i.e. cardiac arrhythmia) which could be used for various botanical materials depending on what type of disorder the botanical material is useful for. (Col. 23, Sec. 5.4.1.). Khwaja, however, does not tie Hp extract, nor any other specific botanical, (i.e., Saw Palmetto, Col. 20, line 19; mistletoe, Col. 26, line 2), to any specific assay, but only gives a general list of possible bioassays.

Further, Khwaja goes on to list methods of use of various Pharmaprinted materials. (Col. 27, Sec. 5.7.). Khwaja states that botanical materials which have been subjected to standardization via the Pharmaprinting method may be useful for those disease states that are already known to be associated with a particular botanical drug. (Col. 27, line 37-38). Khwaja, then gives a general list of those various disease states as well as various therapeutic indications.

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(Col. 27, line 40- Col. 28, line 26). Finally, Khwaja takes specific disease states and therapeutic indications from this general list (i.e., mild-to-moderate depression, antiviral, wound healing, etc.) and identifies them as specific disease states and therapeutic indications for which St. Johns Wort (Hp) is indicated. (Col 28, line 27-35). Indeed, Khwaja only associates St. John's Wort with the disease states and indications mentioned at Col 28, lines 27-35 (which are not claimed), and does not teach that it is desirable to use St. John's Wort for the treatment of any other disease. Accordingly, Khwaja does not teach the use of Hp extract to treat any of the claimed health disorders, nor does it teach the use of Hp extract to inhibit T-type calcium channels. Thus, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §102(e).

Claim Rejection under 35 U.S.C. § 103

Claims 1, 8, 10, 23, 30, 39-44 stand rejected under 35 U.S.C. §103(a) as being obvious over Khwaja et al.

The Examiner contends that the above claims are obvious in view of Khwaja et al.

In response, Applicants maintain that the claimed method for treating arrhythmia, as well as the other claimed health disorders, is not rendered obvious in view of Khwaja et al. Indeed, the Examiner has provided no motivation or suggestion to modify the teachings of Khwaja to use Hp extract to treat the claimed health disorders. Moreover, there is no motivation or suggestion to provide a method of inhibiting T-type calcium channels by administering Hp extract in

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accordance with the claimed invention. The general statement that “botanical materials are useful for any disease state for which a botanical drug is associated” (Col. 27, line 37-38), followed by a laundry list of disease states and conditions, does not suggest that Hp extract or any specific botanical material could be used to treat all of the listed health disorders. Especially when such a statement is qualified by a specific listing of those conditions for which Hp extract is indicated (which list does not include the claimed health disorders). (Col. 28, lines 27-35). That fact that a botanical drug can be used to treat some disease, does not suggest that it would be useful to treat any other disease which happens to be treatable with a different botanical drug. Indeed, there are great number of botanical drugs which have different properties and compositions, and which exert a wide range of various effects depending on such characteristics. A skilled artisan would not have a reasonable expectation of success that Hp extract would be useful for inhibiting T-type calcium channels and for treating the claimed health disorders based on the limited teachings of Khwaja.

Moreover, as Applicants stated in their last response, filed January 30, 2004, at best, it may have been “Obvious to try” using another botanical materials, such as an extract of Hp, to treat one of the listed diseases/conditions associated with botanical materials generally, until one possibly arrived at a successful result. Indeed, that is the most that a person of ordinary skill in the art could have garnered from Khwaja, since Khwaja gives no direction as to which of the many possible choices is likely to be successful. However, “Obvious to try,” is not the correct standard for determining obviousness under U.S. patent law and does not support a *prima facie*

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case of obviousness. Further, a skilled artisan would not have a reasonable expectation of success without more guidance.

The Examiner further states that the effective amount of Hp extract sufficient to treat the claimed health disorders could be obtained through routine experimentation since the range is broad to begin with. Applicant assumes that the Examiner is directing this remark toward claim 10.

In response, Applicants submit that Khwaja gives no direction or suggestion regarding which of the many possible choices for dosages would satisfy an effective amount of Hp extract sufficient to treat the claimed health disorders and sufficient to inhibit T-type calcium channels. It follows that a person of ordinary skill in the art would not be able to determine what amount of Hp extract would be effective to properly function as a T-type calcium channel blocker and inhibit T-type calcium channels, in order to treat arrhythmia and the other claimed health disorders merely by studying the teachings of Khwaja. Khwaja does not suggest or give any direction as to what would constitute an effective dose of Hp extract to treat the claimed health disorders and to inhibit T-type calcium channels because it does not teach or suggest the claimed therapeutic use of Hp extract. This is true for the broadest range claimed in new claim 48, as well as for the more narrow range claimed in new claim 64. Thus, applicants submit that the claimed invention is not rendered obvious in view of Khwaja.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §103(a).

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Applicants further submit that Khwaja does not teach or suggest a method of inhibiting T-type calcium channels by administering Hp extract in accordance with new claims 45-64. As mentioned above, new claims 45-64 are directed, *inter alia*, to a method of inhibiting T-type calcium channels in a patient's cells and treating the claimed health disorders associated with T-type calcium channels via such inhibition. Inhibiting T-type calcium channels is a novel and unexpected therapeutic use of an Hp extract. As discussed and explained in the interview, Applicants submit that all of the claimed health disorders are related in that they are all health disorders in which T-type calcium channels are implicated. Indeed, they are all associated with T-type calcium channels and affected by T-type calcium channel blockers. Applicants direct the Examiner's attention to the attached articles and publications, some of which were also cited on page 2 and 3 of the present application. The articles show that T-type calcium channel blockers are known in the art (e.g. Mibepradil), and they describe some of the structural and functional characteristics of T-type calcium channel blockers. These articles also show that T-type calcium channel blockers are known to be useful for treating some of the claimed health disorders and that such health disorders are associated with T-type calcium channels (See, e.g., "Calcium Channel Blockers," page 7). They also describe some of the characteristics of T-type calcium channels.

Thus, because Khwaja does not teach or suggest a method of inhibiting T-type calcium channels by administering Hp extract in accordance with the claimed invention, Applicant submits that the claimed invention is not anticipated or rendered obvious by Khwaja.

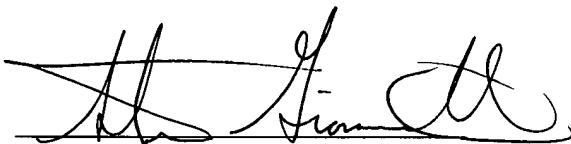
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Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the above rejections.

In light of the above remarks, the presentation of new claims 45-64, and the substance of the personal interview conducted March 2, 2005, Applicants believe that the Examiner's rejections set forth in the March 16, 2005 Office Action have been fully overcome and that the present claims fully satisfy the patent statutes. Applicants therefore believe that the application is now in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

No fee is believed due in connection with the filing of this Amendment. If however, any fee is deemed necessary, authorization is hereby given to charge such fee, or credit any overpayment, to Deposit Account No. 02-2135.

Respectfully submitted,



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Attachments: Examiner Interview Summary
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Cremers B. et al., J. of Cardiovascular Pharmacology, (1997) Vol. 29(5), 692-6.
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